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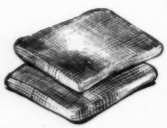

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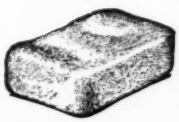

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1. Hutcheson, J. M.: Management of Cardiac Failure. *Virginia Med. Monthly*, 74:458, Oct., 1947.
2. Noth, P. H.: Pick's Disease: A Record of Eight Years' Treatment with Salyrgan, Ammonium Nitrate, and Abdominal Paracentesis. *Proc. Staff Meet. Mayo Clin.*, 12:513, Aug. 18, 1937.

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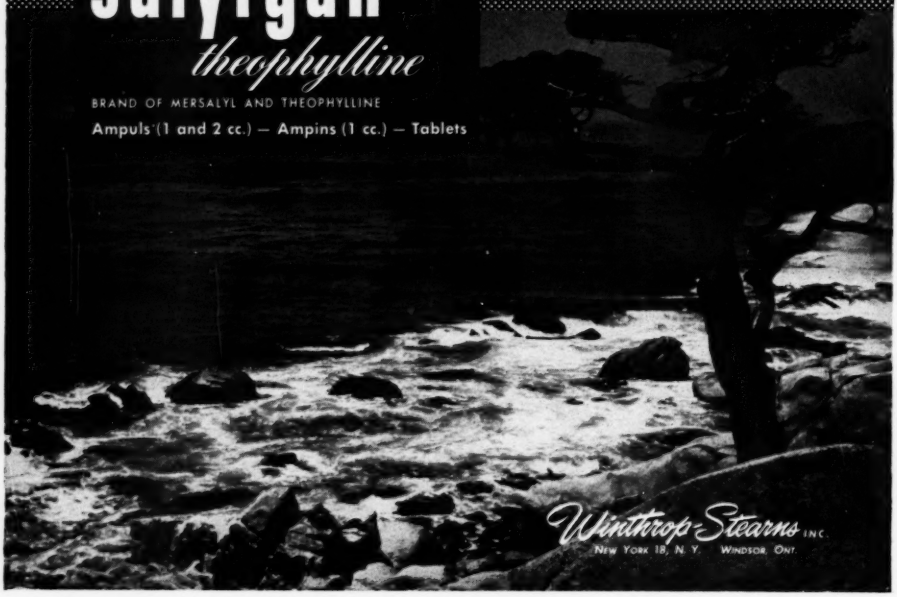

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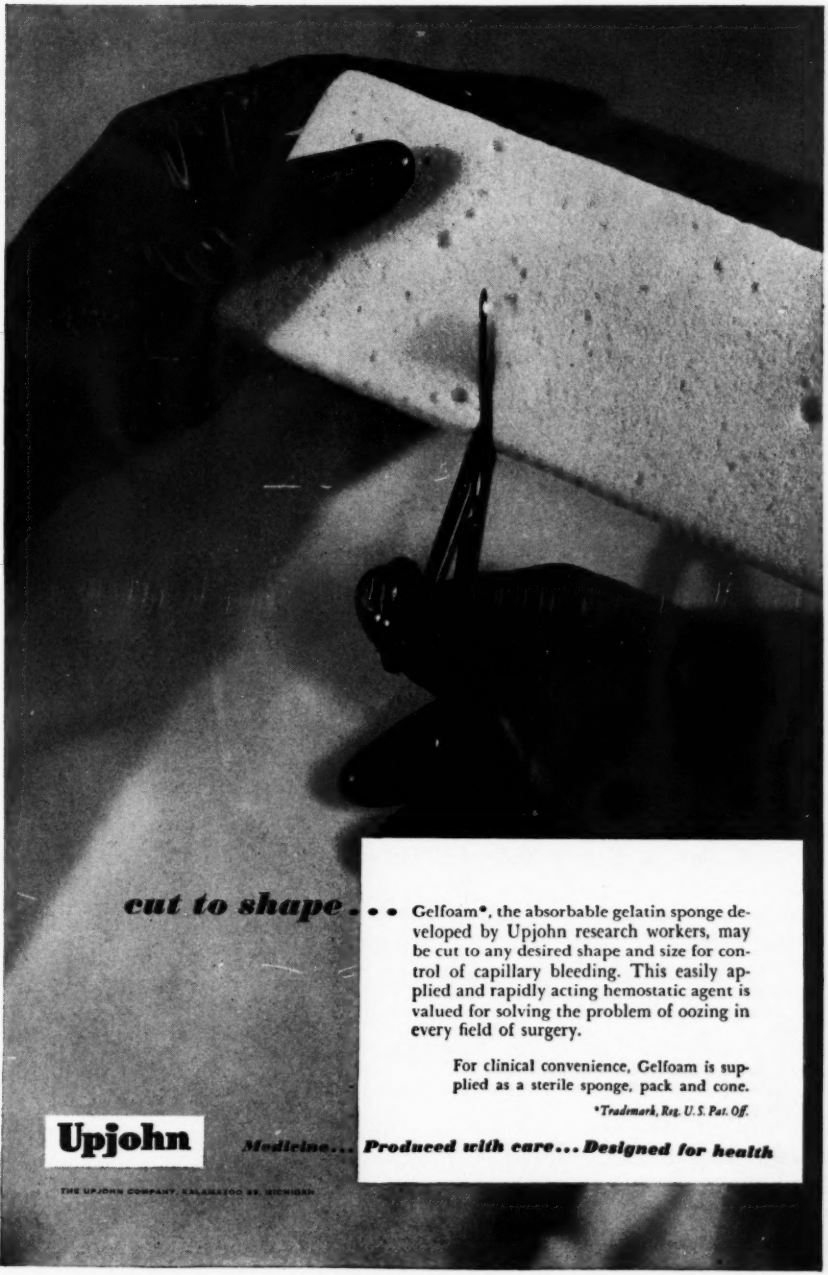
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NORM

Normal schedule of development (auxodrome) plotted on Wetzel Grid.[1]

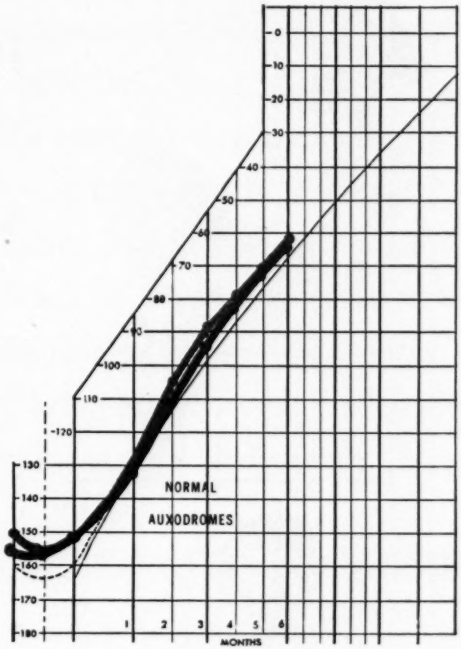
CURVE A

Composite Wetzel Grid auxodrome of 60 unselected infants on S-M-A from birth to 6 months of age.

CURVE B

Growth data, recomputed on Wetzel Grid, based on "selected subjects, most of whom were favored by environment;"[2] age: from birth to 6 months.

1. Wetzel, N. C.: J. Pediat. 29:439, 1946.
2. Jackson, R. L., and Kelly, H. G.: J. Pediat. 27:215, 1945.



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* Hamblen, E. C.: Some Aspects of Sex Endocrinology in General Practice, North Carolina M. J. 7:533 (Oct.) 1946.

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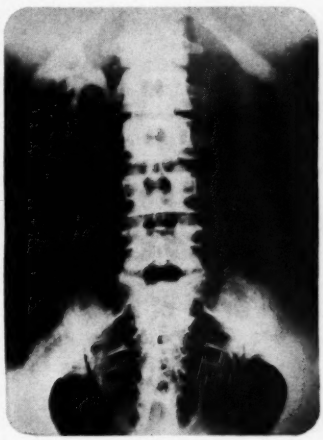

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1. Thewlis, M., and Gale, E. T.: Ambulatory Care of the Aged, Geriatrics, 5:331 (Nov.-Dec.) 1950.

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PROTEIN	32 Gm.	VITAMIN A	3000 I.U.
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CARBOHYDRATE	65 Gm.	RIBOFLAVIN	2.0 mg
CALCIUM	1.12 Gm.	NIACIN	6.8 mg
PHOSPHORUS	0.94 Gm.	VITAMIN C	30.0 mg.
IRON	12 mg.	VITAMIN D	417 I.U.
COPPER	0.5 mg.	CALORIES	676

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Effective against many bacterial, and rickettsial infections, as well as certain protozoal and large viral diseases.

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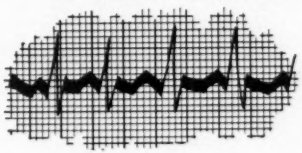

The Internist today is less concerned than in former years over cases of pneumonia. Once highly fatal, this disease has been all but conquered by modern chemotherapy. For many pneumonias—bacterial, rickettsial or viral—aureomycin is often a preferred drug.

Packages

Capsules: Bottles of 25 and 100, 50 mg. each capsule. Bottles of 16 and 100, 250 mg. each capsule.
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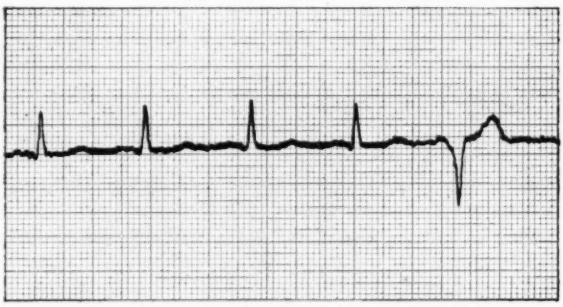
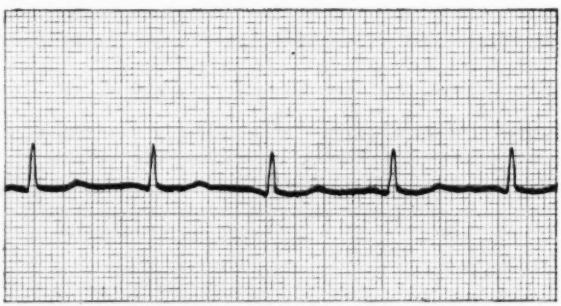
Oral PRONESTYL
in ventricular premature contractions



Lead I. Control tracing, ventricular premature contraction.



Lead I. Tracing one week later; patient maintained on 2 Gm. Pronestyl per day. Normal sinus rhythm.

....PRONESTYL *Hydrochloride*

less toxic than quinidine

Indications and Dosage

IN CONSCIOUS PATIENTS

For the treatment of ventricular tachycardia:

Orally: 1 Gm. (4 capsules) followed by 0.5-1.0 Gm. (2 to 4 capsules) every four to six hours as indicated.

Intravenously: 200-1000 mg. (2 to 10 cc.). *Caution*—administer no more than 200 mg. (2 cc.) per minute.

Hypotension may occur during intravenous use in conscious patients. As a precautionary measure, administer at a rate no greater than 200 mg. (2 cc.) per minute to a total of no more than 1 Gm. Electrocardiographic tracings should be made during injection so that injection may be discontinued when tachycardia is interrupted. Blood pressure recordings should be made frequently during injection. *If marked hypotension occurs, rate of injection should be slowed or stopped.*

For the treatment of runs of ventricular extrasystoles:

Orally: 0.5 Gm. (2 capsules) every four to six hours as indicated.

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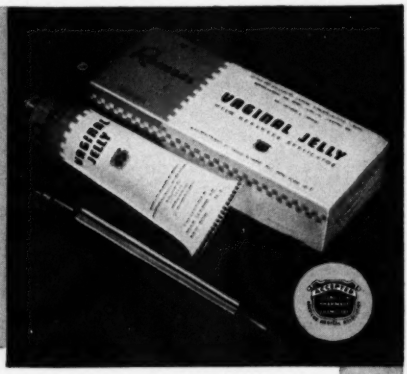

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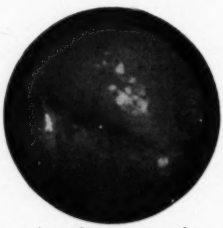

Photo taken after insertion of "RAMSES" Vaginal Jelly. Os occluded.

Photo taken ten hours after coitus. Occlusion still manifest.

Jelly stained with nonspermatocidal concentration of methylene blue for photographic purposes.

gynecological division

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Results of therapy in 32 obstetrical and gynecological cases

	ORGANISM	NO. OF CASES	RESULTS		
			GOOD*	EQUIVOCAL	POOR
No organic or obstructive disease					
	B. coli	15	14	1	0
	A. aerogenes	4	4	0	0
	Aerobic diphtheroids	3	2	1	0
	S. albus	2	2	0	0
	Aerobic non-hemolytic streptococcus	2	2	0	0
	Ps. aeruginosa	1	0	1	0
With organic or obstructive disease					
	Ps. aeruginosa	3	1	0	2
	P. vulgaris	1	0	1	0
	A. aerogenes	1	1	0	0
	TOTALS	**32**	**26**	**4**	**2**

Douglas, R. G.; Ball, T. L., and Davis, I. F.: California Med. 73:463 (Dec.) 1950

*"*A good result was recorded when in 72 hours or less the temperature fell to normal, the pyuria cleared, a negative culture was obtained and the patient was symptom-free."*

CRYSTALLINE

Terra

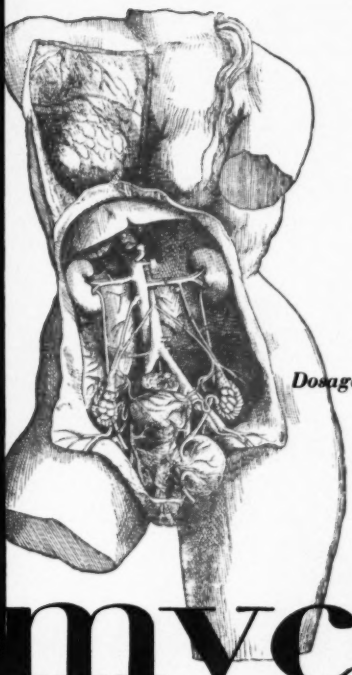
"The drug is tolerated by mouth and no serious side-reactions occur."

Douglas, R. G.; Ball, T. L., and Davis, I. F.: California Med. 73:463 (Dec.) 1950.

Antibiotic Division

OBSTETRICAL AND GYNECOLOGICAL PATIENTS

"prompt and effective" response



"In cases in which there is no organic or obstructive disease, the response to Terramycin as a urinary antiseptic is prompt and effective."

"The patients with pyelitis of pregnancy or simple postoperative cysto-ureteritis responded very promptly....There was a prompt drop in temperature, disappearance of pyuria and bacilluria, and symptomatic relief."

Douglas, R. G.; Ball, T. L., and Davis, I. F.: California Med. 73:463 (Dec.) 1950.

Dosage: 2 Gm. daily by mouth in divided doses q. 6 h. is suggested for most acute infections. In severe infections, a high initial dose (1.0 Gm.) or higher daily dosages (3 to 6 Gm.) should be used. Treatment should be continued for at least 48 hours after the patient's temperature has become normal and acute symptoms have subsided.

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...plenty of citrus fruit

References

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11. Stevenson, S. S.: J. Pediat., 31:616, 1947.

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THE USE OF FAT IN A WEIGHT REDUCING DIET*

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Lavoisier, in the latter part of the eighteenth century, established, in principle, that the law of the conservation of energy applies to the biochemistry of nutrition. Thus, the foundation was laid for a scientific knowledge of the energy transformations within the body, known as metabolism. One of the things Lavoisier knew was that the ingestion of food increases the heat production of the body; and this scientific datum, more than one hundred and fifty years old, forms the core of the thesis which it is my honor to present to you today.

The energy of the body is derived entirely from food. This means that, when physical work is done, chemical energy has been transformed into mechanical energy. To accomplish this transformation, the human body is endowed with intricate chemical enzyme systems; and the energy required for the operation of these is also derived from food.

The chemical energy residing in the food we oxidize is ultimately accounted for as heat, in most part whether we accomplish physical work or not. The situation is roughly analagous to that of a stove. Fuel is put in and burned; heat is produced and this radiates to the surroundings.

The human body possesses an elaborate radiator system which is controlled with thermostatic precision. It responds to conditions exterior to the body and also to conditions existing in the interior, with the result that the body temperature is ordinarily kept within narrow limits. It is to the internal conditions affecting this radiator mechanism that I would like to direct attention.

If much food is eaten and oxidized, much heat is produced and radiated. If little food is eaten and oxidized, there is less heat production. Whether much or little heat is produced, the temperature of the body, taken as it ordinarily is at the periphery, is fairly constant. The thermal gradient from within, out, may be steep or almost level, for the temperature regulating mechanism responds effectively to varying quantities of heat production in the interior.

Although the temperature of the body is controlled with a fine degree of precision, there is not, as far as is known, a control of heat production in any way similar. Heat production increases when physical exercise, largely of a voluntary character, is performed. It is increased under certain environmental conditions which stimulate the thyroid and the adrenal glands and also the appetite. For the person who engages in little vigorous exercise and whose clothing protects him against great temperature changes, however, the essential influence on heat production is the ingestion of food. When food is eaten, heat production begins to rise within an hour and continues for several hours at an accelerated rate.

Food which is eaten and not oxidized is stored in the body as fat. It is obvious, therefore, that, if a person is gaining weight, he is eating some food from which he is obtaining no energy. It has commonly been assumed, without scientific foundation, that given sufficient food, the energy requirements will be optimally fulfilled and that any excess will be converted to fat. This theory assumes a precise regulatory control over heat production which no scientific investigation has yet disclosed. Acting, however, on the theory that such a regulatory mechanism exists, calculations of energy requirements have been made by adding the figure determined from the respiratory equivalent in the resting, fasting state to an estimate of

*Read before the Medical Society of Delaware, Dover, October 4, 1950.

the energy needed for physical work. The sum of these has been believed to represent an individual's caloric needs; and students of home economics have become very proficient in translating this figure into terms of food. If a person eats more than this figure calls for it is expected that he will gain weight. If, then, he is given a diet of lower caloric value than his calculated requirement, it is predicted that he will lose weight; and if the predictions of the calculator are not fulfilled, the patient is suspected of being a glutton on the sly or else of having found some way of violating the laws of thermodynamics.

The basis on which such a view rests is entirely theoretical and the nutritional data supporting it are meagre and conflicting. In reviewing the matter critically one can hardly avoid the conclusion that the essential basis of it is a strong conviction, a matter of faith.

Although no physiological mechanism regulating the production of heat has been found, something is known of circumstances which limit the ability of the body to convert food into energy and which, indeed, may cause energy production to fall far short of the optimum. Details which throw light on these matters have become available to us since the discovery of deuterium. This paved the way for an extensive use of isotopes as tracer elements in physiological investigations. We now have a concept of the tissue structure of the body which varies greatly from concepts of the past. The protein tissue structures are not static, but are in a continual state of exchange, new protein being laid down and the old removed.[1] Fat deposits of the body, also, are maintained by a balance of forces:—those which are continually depositing new fat and those which are mobilizing the old. An even greater condition of flux exists in regard to the carbohydrate stores of the body, meagre as those are. It is to be expected, in considering this dynamic state of affairs, that the energy requirements for optimal functioning of all these biochemical exchanges might well be greater than was previously thought, and that they should exceed the mere requirement for keeping the body warm. Energy is needed for growth of the body and, when full growth is achieved, energy is needed to prevent deterioration.

There are two factors which can limit the production of energy from food, once it has been ingested and absorbed. One is the capacity of the tissues to oxidize a food substance and the other is a mechanism which withholds the food substance from the tissues. It is enlightening to examine these two factors in their relation to the major dietary sources of energy—carbohydrate and fat.

The ability of the tissues to oxidize carbohydrate is limited by their capacity for breaking down pyruvic acid to the two-carbon intermediaries which enter the tricarboxylic acid cycle for the final and complete combustion of carbohydrate to carbon dioxide and water.[2,3] For this link in the chain of enzyme reactions involved in the oxidation of carbohydrate, thiamine is needed[4] as well as biotin[5] and we know not what else of exogenous source. Even when the most favorable enzymatic conditions exist, the capacity of the tissues to break down pyruvic acid can be overwhelmed[6] with the result that pyruvic acid returns to the liver, where it is converted to fatty acids.[7]

The ability of the tissues to oxidize fat is, in contrast to carbohydrate, unlimited. Fat itself, in the triglyceride form familiar to the dinner table, is not directly combusted; but the fatty acids into which triglyceride fat is easily hydrolized, are utilized by the tissues for energy in preference to carbohydrate[8]. Even more striking than this is the ability of the tissues to oxidize the ketone bodies which the liver normally forms from fat. Stadie has estimated that the peripheral tissues can burn fat, as ketones, in an amount four to six times an individual's basal requirement[9]. In a person whose basal requirement was 2000 calories this would mean that his tissues could oxidize ketones in an amount representing 8,000 to 12,000 calories. It is hardly possible that such an amount would ever be presented to the tissues for their consumption; and it is not to be wondered at that the human body is endowed with a mechanism which will store this excellent fuel in considerable quantities.

This view, that fats are the preferred fuel of the tissues, that they are oxidized more readily than carbohydrates and without the aid of carbohydrates, is a physiological dis-

covery for which we are indebted to the investigations made possible by tracer elements. It represents a complete reversal over views previously held. One of the most unfortunate days in the history of modern medicine was the day that Macleod made the famous statement which runs as follows: "If the carbohydrate fires do not burn briskly enough, the fat is incompletely consumed; it smokes, as it were, and the smoke is represented in metabolism by the ketones and derived acids."[10] That imaginative statement, made by a great physiologist, has so laid hold on the minds of generations of medical graduates that the experimental work of Stadie and others seems to have had little effect. To those who repeatedly quote Macleod's statement to me I am sometimes tempted to say: "Do you know fat burns?" Fat burns in the body, hot and clean!

Thus, modern biochemical investigations indicate that the tissues have a limited capacity to burn carbohydrate and that when that substance is presented to the tissues in excess of that capacity it will be broken down as far as the pyruvic acid stage and then converted to fatty acid; while fat, in the form of fatty acids and ketones, will burn in an unlimited amount, as long as it is presented to the tissues.

Now, it might well be asked why, when pyruvic acid is converted to fatty acid, is it not then burned as such by the tissues. There is no doubt that it is and that this is the way in which much dietary carbohydrate is made use of in the body, particularly during physical exercise. But now we must consider a particular balance of forces—those which promote the formation and storage in the body of triglyceride fat, and those which are antagonistic to this, which promote the mobilization of triglyceride fat and its breakdown to the easily combusted fatty acids and ketones. Both of these forces are operating all the time; and any weight gain or loss in an individual is determined by that one of these forces which is predominant. It is helpful to think of each of these two forces as a physiological situation in which various agents play their parts.

In the physiological situation which promotes fat storage, the leading role is played by carbohydrate. Now, the capacity of the tissues to oxidize carbohydrate is limited, as has been mentioned, with the result that greater or less amounts, when they have reached the pyruvic acid stage, are turned back to the liver. At the same time, carbohydrate stimulates the pancreas to an increased production of insulin. Insulin, acting on the pyruvic acid which has been returned to the liver, stimulates its conversion to fatty acid and then promotes the deposition of this, as fat, in the adipose tissues of the body.[11, 12] This is the fat storage mechanism, which operates normally in the body and is in operation continually. It can easily be seen, however, that great amounts of carbohydrate in the diet may so increase the activity of this fat storage mechanism that more fat will be deposited in the tissues than is being removed. No doubt, this mechanism has subserved the race in preparing for times of famine. In our day, such physiological preparation for a famine which never arrives, leads the way to obesity and all its attendant ills. Notable among these ills is the diabetic state, in which the fat storage mechanism finally fails.[13]

While overconsumption of carbohydrate appears to be the cause of obesity, it is not a simple matter to state what constitutes overconsumption in any individual case. It all depends on the capacity of a person's tissues to break down pyruvic acid. Many factors could conceivably affect this rather vulnerable enzymatic step in the oxidation of carbohydrate. Among them might be cited the influences of heredity, infection, pregnancy, surgical anesthesia, allergy and increasing age. We have no assurance that the ability to break down pyruvic acid is the same in all sorts and conditions of people. On the basis of clinical observations alone, I am willing to venture the statement that it is not the same and that, in some cases, a very small amount of carbohydrate in the diet will so overwhelm the capacity of the tissues to oxidize pyruvic acid that an individual will increase in weight even though the total caloric value of the diet would not seem excessive. Aiding and abetting the storage of fat in such a case would be a concomitant sensitivity of the insulin apparatus, with a greatly increased production of insulin. Even a rather small

amount of carbohydrate could, therefore, constitute over-consumption of that substance. Thus, the cause of obesity becomes, in many cases, an inability to oxidize sugar and starch.

A person who lacks the ability to oxidize sugar and starch stores those dietary substances as fat instead of converting them to energy. Heat production in the body suffers, while the individual becomes obese. If, as is often the case, obesity prepares the way for diabetes and failure of the fat storage mechanism, ketones as well as carbohydrate are lost in the urine. This is an economic waste.

Turning our attention now to the physiological situation which promotes fat mobilization, we find that the leading role is played by the anterior pituitary fat-mobilizing principle.[14]

This is in constant operation. Some triglyceride fat in the adipose deposits of the body is continually being taken up by the blood and oxidized in the liver to ketone bodies, which the peripheral tissues combust readily.[9]

When a person maintains constant weight, whether he is fat or lean, there is a balance between the forces which are storing fat and those which are mobilizing it. It has been observed that many obese persons maintain their weight, yet eat very little.[25] Furthermore, the fat man uses some of the energy he produces to keep his fat alive.

When the objective is for a person to lose weight it is necessary to bring about the physiological situation in which the fat mobilizing process predominates over the fat storage process. The first essential in this is to hold the dietary content of carbohydrate well within the capacity of the tissues to oxidize the pyruvic acid which is formed from it. If this is done, all the carbohydrate ingested can be completely combusted to carbon dioxide and water. Restriction of carbohydrate also removes the stimulus from the insulin mechanism, so that the fat storing activity of insulin will be at a minimum. The anterior pituitary fat-mobilizing principle will then predominate over the fat storing forces. Fat will be mobilized from the adipose deposits of the body, oxidized to ketones in the liver and circulated to the tissues in this easily combustible form. By whatever dietary method reduction of obesity is accomplished, this normal mechanism of ketogenesis must be brought into play, for it has long been known that, while carbohydrate can be readily converted to fat in the body, fat can not be converted into carbohydrate in any significant amount.[15]

The physiological situation which promotes weight loss can be brought into play by complete starvation, which increases ketogenesis.[16] It can be done, also, in a hit or miss fashion, by low calorie diets, which are a form of semi-starvation. Some of the more rigorous low calorie diets practically amount to starvation.[17] Often, in treating obese patients by such a method it seems that the margin between safety and effectiveness is a very narrow one. In some cases it may well be questioned whether such a margin exists. Energy production in the body is quantitatively reduced, for there is no guarantee that adipose deposits will be mobilized on schedule to make up the deficit between the optimum energy requirement of the body and the lowered caloric intake. Indeed, it must be obvious to all who have dealt with the problem of obesity that patients adhering to low calorie diets are often weak and tired, while the weight chart shows that little or no adipose tissue is being mobilized and burned.

The safest and most effective method of weight reduction is to eliminate carbohydrate from the diet completely and to allow an *ad libitum* intake of protein and fat. The physiological situation which promotes fat mobilization is brought into play with great effectiveness by this means. Protein supplies the lipotropic factors necessary for the phospholipid turnover in the liver[18] and, through gluconeogenesis, the glycogen required by the nervous system. Ketogenesis is active, as it is in any method by which weight is reduced. If it happened that ketone bodies were formed in greater abundance than could be taken up by the tissues, they would be drawn off, harmlessly, in combination with ammonia, through the kidneys. The kidneys form ammonia from urea, and this is manufactured in plentiful amount through deamidization of protein by the liver.

When such a high protein, high fat diet

is used, it has been found advantageous to prescribe nine ounces of lean meat and three ounces of fat, cooked weight, at each of the three meals of the day, with the patient at liberty to take more, if he chooses, in that proportion—three parts of lean to one of fat. A loss of weight of twelve pounds a month is usually accomplished on such a regimen. When normal weight is reached, the weight loss stops.

A modified form of this diet, containing six ounces of lean meat and two of fat, or more in that proportion, at each of the three meals of the day, with the addition of an ordinary serving of one of the less concentrated carbohydrate foods, is effective in most cases. The weight loss, however, is usually slowed down to seven pounds a month. The sheet of instructions given to patients on such a diet is as follows:

A Diet For Obesity

With this diet you follow a definite routine which is as important as the diet itself. Have a regular hour for going to bed. Set your alarm clock for eight hours sleep, never a minute more than that, and allow time for a thirty minute walk before breakfast. It is not necessary to walk fast, but it is necessary to walk the full thirty minutes regularly.

Breakfast, lunch and dinner are all the same type. You eat three big meals a day and lose seven pounds of excess weight a month.

First course of each meal: One-half pound or more of fresh meat with the fat. This part of the diet is unlimited. You can eat as much as you want. The proper proportion is three parts lean to one part fat. Most of the meat you buy is not fat enough, so get extra beef kidney fat, slice and fry it to make up the proper proportion. Good meats are roast beef, steak, roast lamb, lamb chops, fresh pork and pork chops. Hamburger is all right if you grind it yourself just before it is cooked. Season the meat with black pepper before it is cooked or use paprika, celery seed, lemon, chopped parsley or celery tops, or other flavoring which does not contain salt.

Do not use the least particle of salt. Do not use foods containing salt, such as soup, bacon, smoked ham, canned chicken, canned fish, frankfurters, bologna, canned or spiced meat, or salted butter.

Second course of each meal: This part of the diet is limited. At each meal you have a choice of an ordinary portion of any one of the following:

White potatoes, boiled, or home fried.
Sweet potatoes
Boiled rice
Half grape-fruit
Bunch of grapes
Slice of melon
Banana or pear
Raspberries or blueberries

At the end of each meal have a cup of black coffee or clear tea without sugar. Do not use saccharine.

Be sure to drink six glasses of water every day before five o'clock. Your only other beverage is half a lemon in a glass of water.

Have a physical examination by your doctor before starting on the diet and have him check up at regular intervals. Weight must be regulated completely to normal before other foods can be added or you will quickly gain the weight you have lost. After the weight is normal you can test out how far you can depart from the diet without gaining weight.

Note particularly that this diet contains no bread, flour, salt, sugar, or alcohol.

A report of results in the use of these principles of weight reduction has been made.[19] Twenty overweight individuals lost an average of over 21 pounds each in an average time of three and a half months. A year later it has been found that the average weight gain since that loss has been less than two and a half pounds. All of these individuals are in good health at the present time.

The morning walk is essential in enabling a person to eat the requisite amount of fat. The entire success of the diet depends on eating enough fat. Otherwise, the patient would be on a mere low calorie diet, with all the disadvantages such a diet entails.

Meat fat is chosen because it is lower in cholesterol than other animal fats commonly used[20] and there appears to be less allergy to it than to vegetable fats. There are many advantages in a high fat diet which can not be enumerated here.[21,22] Fat is helpful in preventing gall bladder disease because it stim-

ulates the gall bladder to complete emptying.[23] Fat has been suggested as useful in the treatment of atherosclerosis because it is a good solvent for cholesterol.[24]

One of the chief advantages of this diet is that it maintains energy production, for the tissues are supplied with the kind of fuel which they are best adapted to use and the only limitation on energy production is the very natural one of a person's appetite. This, it seems, is of significance in the present day, when we are greatly concerned with the metabolic derangements underlying the socalled degenerative diseases. There is much uncertainty and confusion as to what those metabolic derangements are and what can be done about them. Amid all this confusion, however, there is one basic and inescapable fact. Energy is needed for the successful operation of the multifold biochemical exchanges involved in metabolism, a term which Graham Lusk defined as "the flame of life." May I wish for you, gentlemen, that that flame may burn brightly and long.

SUMMARY

A review of the intermediary metabolism of carbohydrate and fat, as determined by biochemical investigations with tracer elements, indicates that carbohydrate should be severely restricted in weight reduction diets. Energy production should be maintained by a liberal intake of dietary fat in conjunction with protein. Details are given concerning such a diet, which has been used successfully for reduction of weight. The use of this diet as a means of preventing atherosclerosis and gall bladder disease is discussed.

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DISCUSSION

DR. J. R. DURHAM, (Wilmington): Dr. Pennington has presented a most interesting and thought-provoking paper, and I believe this type of paper, dealing with a difficult problem which we have faced in our practice and which offers a new solution, should be encouraged. Here we have presented for us a new theory on the cause of obesity and its treatment. I want to congratulate Dr. Pennington for his temerity in presenting it, but I want to disagree with some of his conclusions, at least in part.

1. "The chemical energy of food we oxidize is ultimately accounted for as heat whether we accomplish physical work or not." Untrue. The energy for work does not appear as heat.

2. The implication that heat production is proportionate to the amount of food taken in cannot be accepted. Actually, on usual diet, the so-called specific dynamic effect from food amounts to 250 calories per 24 hour period, plus or minus 50 calories depending on meal size. Newburg and co-workers, after careful study of the total heat production, found no evidence that either the basal or total metabolism was stimulated by superalimentation.

3. Despite what Dr. Pennington says about calories, the simple principle—that obesity is invariably the result of a disproportion between the inflow and outflow of energy—remains unchallenged. Persons who ingest fewer calories than they produce lose weight. The human body does not violate the law of conservation of energy.

4. If some individuals have greater difficulty in oxidizing small amounts of carbohydrate, the carbohydrate would be excreted in the urine as sugar and not stored as fat.

5. The statement that many obese persons maintain their weight yet eat very little is certainly not accepted by authorities in metabolism. I refer you to the vast amount

of evidence published by the Sage Laboratories under the direction of Drs. Lusk and DuBois.

6. The author's contention, indeed the mainstay of the entire thesis, that fats are the preferred fuel of the tissues and that they are oxidized more readily than carbohydrate has—so far as I have been able to determine from my readings of Stadie, Newburg and others—no basis in clinical or experimental research.

7. The statement that the kidneys form ammonia from urea has never been shown to occur, despite repeated search for this by many investigators.

And now we come to a most important point. How many calories are ingested by the patients on Dr. Pennington's diet? If the modified diet of 6 ozs. of lean meat and 2 oz. of fat is used, something less than 1800 calories a day are supplied. This would cause anyone to lose weight. I hope Dr. Pennington will have an opportunity in the future to determine the actual caloric consumption of patients on this diet.

I will not say anything concerning the possible vitamin deficiency of this diet except that I do not think it is a serious criticism.

In the present state of our knowledge concerning atherosclerosis, I do not believe the fat diet can be recommended for the prevention of this degenerative process. In the same vein, a high protein diet can be harmful in the presence of any kidney involvement. Certainly a high protein diet would not be acceptable in a patient with any nephritic state.

In closing, let me say again that I am very interested in Dr. Pennington's presentation. I would like to see more data on the actual calories ingested. Perhaps a control setup with one group on Dr. Pennington's diet, with a measured or weighed diet, and another group, control group, on the same amount of calories but, let's say, on the common low calorie weight reducing program, can be studied. Perhaps the author has found a new approach to the problem of obesity, but it must be substantiated, and it must be based on sound physiological principles.

Dr. L. B. Flinn, (Wilmington): Dr. Durham has mentioned that this is a most unusual approach in the way of a diet for obesity. Many of the statements which Dr. Pennington made seem to me quite sweeping and without sufficient foundation from an investigative source. I have not heard the paper before and cannot recall many of the statements which I would consider at least controversial.

From what knowledge I have of the carbohydrate metabolism, which has been largely from reading, it has been my impression that although carbohydrate can be metabolized and finally burnt and used in the form of pyruvic acid, or go through the carboxylic cycle, it is certainly not in accordance with Stettin's work considered to be the usual procedure. That is a method for combustion of carbohydrate which the body can call upon in times of need and stress.

The diet suggested certainly seems to me to have certain practical significance. I am sure patients on this diet do lose weight. I am not impressed that they lose more weight than other adequate low calorie diets.

The idea of a high protein diet is not new. Perhaps there is some advantage in a dynamic action of protein itself. All patients, I think, tend to lose weight on any low sodium, low salt diet. Hypertensive cases who are put on a low sodium diet, without any particular reference to protein, carbohydrate, or fat, lose weight.

I would suspect that any patient who is given a large amount of meat and meat fat, as much as he wants, soon finds he doesn't want a great deal. Most people cannot keep up a very large appetite for animal fat if it is thrown at them three times a day. So that, as Dr. Durham suggested, the end result of this diet, I would suspect, is really a fairly adequate low calorie diet with sufficient protein to provide energy and to provide easy carbohydrate stores when needed.

It is certainly an expensive diet, particularly in this day, which again would be one of its drawbacks.

There are many other details which are tempting to discuss but which would take too long today. I would like to say one more word, and I have previously mentioned this to Dr. Pennington, that even if we should assume that this is a good diet, and it may turn out to be such, I would like to say that I was most disappointed and shocked to see

the display given this diet in *Holiday* magazine, representing the work of one of the most outstanding industrial medical departments in the country. I have always been very happily associated with the individuals in the medical department of the duPont Company, and I hope I still will. But I cannot conceive of any reason why such an organization would allow a splurge like what was displayed in *Holiday* magazine, and I'm certainly sorry that it occurred.

DR. PENNINGTON: I wish to compliment Dr. Durham and Dr. Flinn for their scientific detachment in reviewing a paper which opposes some widely held concepts; and I thank them for recognizing that this is a serious effort to help solve an urgent medical problem.

I think we are all in accord with the simple principle that obesity results from a disproportion between caloric intake and output. What I have attempted in this paper is to point out that within the framework of that simple principle are intricate matters which must be taken into account.

The two diets I have described contain upward of 2430 calories, according to the tables of the U. S. Department of Agriculture. The statement that people lose weight on such diets has aroused some amazement and, no doubt, some incredulity. I sympathize with that incredulity and offer to direct you to its cause.

We have all been indoctrinated with a simple, mechanistic formula which places complete faith in a term "caloric requirement." Ancel Keys, in the *J.A.M.A.* this year, pointed out that that term is used widely without clear definition. The "ideal caloric requirement" involves theory which may or may not be correct. The factorial method of estimating it is subject to error; and one matter involved is the accuracy of the BMR reading.

The term, "caloric requirement" is useful in estimating the amount of food necessary to keep a large population group alive, but it has little meaning in any individual case where a physician is trying to help an individual achieve optimum health. Keys has shown that the underfed organism conserves its expenditure. Everyone will not lose weight on 1500 calories, nor on 1100. The 450 calorie diets recommended by Evans and Strang will reduce practically everyone, but that is coming pretty close to starvation. Grafe, in his book, "Diseases of Metabolism", reports cases under close supervision on diets close to that level, who did not lose weight satisfactorily. Contrary to the claims of the low calorie school of thought, low calorie diets have failed under the most rigid experimental conditions. When, as in ordinary practice, the experimental conditions are less rigid, the claim is invariably made that the patient was not following his diet; and this claim is not made on the basis of knowledge. It is a predetermined opinion based on allegiance to a figment of a mechanistic imagination—namely "caloric requirement."

Those who find in this term a simple and final answer to all the problems of obesity save themselves a great deal of trouble. They need never investigate the effects of catalytic agents, enzyme inhibitors, or other variables. They need not consider the energy utilized in endothermal reactions which involve the synthesis of protoplasmic materials and which does not, therefore, figure immediately in calculations of energy output.

To conclude, the low caloric diets based on the principal of caloric requirements are crudely devised in the service of simplicity and must, eventually, go the way of the D/N ratio, a former mainstay of the same school of thought. There are fat people, plenty of them, who are actually starving.

(Ed. Note—See letter page 104)

CANCER OF THE LARYNGO-PHARYNX*

Radical Surgical Resection Combined With Neck Dissection and Esophagoplasty Preliminary Report

JOHN F. HYNES, M. D.,
Wilmington, Del.

Extensive cancer involving both larynx and pharynx presents a difficult therapeutic problem to which there is as yet no satisfactory solution. The medical literature contains many reports of excellent results in the treatment of cancer of the intrinsic larynx: that is, cancer confined within the cartilagenous

*From The Carpenter Memorial Clinic, Memorial Hospital, Wilmington, Delaware. Read before the Medical Society of Delaware, Dover, October 3, 1950.

laryngeal box, whether by partial laryngectomy through laryngofissure, total laryngectomy, or radiation therapy. Reports of cancer involving both the larynx and the adjacent pharyngeal structures are fewer: they are the "inoperable cancers referred for palliative irradiation" by the surgeon, or are included by the radiologist in a series of cases of varying extent and anatomic location, from naso-pharynx and tonsil through base of tongue and larynx to pyriform sinuses and post-cricoid region. We propose to discuss the results obtained in the treatment of cancer involving the extrinsic larynx and/or pharynx, with particular reference to the advanced, "inoperable" extensive cancer involving both organs.

It is almost axiomatic to classify cancer of the extrinsic larynx, especially when the pharynx is involved, as inoperable. (Nielsen[6], Quick[8] and others). Laryngologists who emphasize the curability of laryngeal cancer (80 to 90% in cancer confined to a vocal cord, 50-70% by total laryngectomy for more extensive laryngeal lesions) invariably refer to cancer of the intrinsic larynx. From some of the reports one would assume that such cases are three or four times as common as extrinsic laryngeal and/or pharyngeal cancer, yet other authors report the incidence of the two types to be about equal, and in our own series cancers involving both larynx and pharynx predominate. On the other hand, as Martin[5] has pointed out, radiologists reporting good results in the treatment of laryngeal cancer presumably have a larger proportion of limited lesions in their series. For example, in 1932 Coutard[2] reported from the Curie Institute 27% five year survivals in cancer of the tonsil, hypo-pharynx and larynx. Baclesse[1], reporting from the same institution in 1949, subdivides his cases into anatomic groups: he reports 6% five year survivals for cancer involving the hypopharynx.

The treatment of extensive cancer of the laryngo-pharynx has been the subject of relatively few reports in the surgical literature, particularly in this country. One of the best, that of Wookey[9,10] describes a satisfactory approach, a modification of which was employed in three of the four cases we have treated. Very recently Owen[7] reported 22 cases of pharyngo-laryngectomy with 4 (18%) five year survivors.

The anatomy of the pharynx and larynx must be reviewed for proper understanding of the therapeutic problem. The intrinsic larynx may be considered as the limited area from subglottic region to the vestibular bands; some authors include also the posterior aspect of the epiglottis. The extrinsic larynx is more loosely defined: it includes the epiglottis, aryepiglottic folds, and arytenoids, and usually the post-cricoid region, although the latter is really a part of the pharynx, lying at its junction with the esophagus. The posterior and lateral pharyngeal walls are obviously part of the pharynx. The pyriform sinus is also pharyngeal, but is bounded medially by the arytenoid and aryepiglottic fold. It is our experience that a majority of epilaryngeal cancers are also "epiesophageal": they involve the pharynx as well as the larynx. (Table 1)

This discussion of anatomy is of more than academic importance. It is apparent, both from our own results and the reports in the literature, that cancer involving the hypopharynx is seldom curable by radiation methods (in which it resembles its anatomic continuation, the esophagus). If, then, many if not most cancer of the extrinsic larynx involve also the hypopharynx, it explains the low curability of such cancers, as compared to intrinsic laryngeal cancer where radiation therapy is often very effective, according to Cutler[3], Lenz[4] and others. Furthermore, bulky cancers do not seem to do as well under radiation therapy as do limited lesions, and bulky, everting masses within the pharynx are characteristic of hypopharyngeal cancer.

Results of Radiation Therapy

Thirty-eight cases treated from 1935 to 1949 have been reviewed. One case who refused all treatment, one untreated terminal case, and one case seen only in consultation, were not considered in the series. (Table 1)

Ten cases were classified as confined to the extrinsic larynx, after careful study of the description on the record, yet five of these

TABLE 1

RESULTS OF RADIATION THERAPY 1935-1949

Anatomic location	Total cases	Five year Survival	Radiation Failure	Totally Inoperable	Operable By Radical Resection	Operated after Radiation Failure
Extrinsic, larynx only	10	1(a)	9	4	6	2(b)
Pharynx only	5	0	5	2	3	0
Larynx & Pharynx	23	0	20(c)	12	11	1(d)
	39	1	34	18	20	3

developed proven or presumptive evidence of recurrent cancer in the hypopharynx or cervical esophagus, while the larynx remained healed after treatment, which would suggest that pharyngeal involvement was present but unrecognized on their initial examination. One patient, aged 78, with a lesion only 1.5 cm. in diameter, confined to the superior aspect of the arytenoid, has survived six years following irradiation. One patient with recurrence two years after treatment survives an additional three years following total laryngectomy, and another recurrent one year after irradiation survives two years since laryngectomy. Nine of the ten cases must be classified as failures of radiation therapy.

Five cases with primary disease limited to the pharynx were irradiated. None of these survived more than twenty-five months following treatment.

Twenty-three cases with extensive cancer involving both larynx and pharynx were irradiated. Three are living 3 years, 2 years, and 14 months respectively, apparently well, although the last patient may yet require surgical treatment. One other patient survives 15 months since his original treatment, but has recurrent disease. One other case had radical surgical resection, as described below, and died two later from other causes. There are no five year survivors. The single survivor reported above was one of 21 cases treated prior to 1945 (4.8%).

a) Small (1.5 cm.) non-infiltrating cancer of arytenoid.
b) Case No. 22, recurred 2 years after treatment, has survived 3 years since laryngectomy in 1947.
Case 30, recurred 1 year after treatment, has survived 2 years since laryngectomy in 1948.
c) Three cases are living without recurrence 3 years or less since treatment.
d) Case No. 33, had glosso-laryngo-pharyngectomy for recurrence and survived 2 years, dying without evidence of recurrent cancer.

RESULTS OF SURGICAL TREATMENT

Three cases, not included in the radiation series, have had primary surgical treatment consisting of unilateral radical neck dissection and pharyngolaryngectomy. A skin flap from the side opposite the neck dissection was prepared at this operation and anchored to the stump of the pharynx above and the esophagus below. At a later stage a buried skin tube was completed in the manner described by Wookey, (9,10) and the raw surfaces covered by the skin graft (split thickness). Two of the patients have left the hospital with good swallowing function; the third is almost ready to leave, although his course has been delayed by technical difficulties in constructing the esophagoplasty since his resection also included the hyoid bone and base of tongue. The first radical resection was performed in a case recurrent after heavy irradiation and included practically the entire tongue, so no esophagoplasty was considered practical.

OPERATIVE TECHNIC

Under procaine anesthesia a transverse incision at the level of the hyoid bone extends from the sternomastoid muscle on the uninvolved side to the mastoid process on the side chosen for neck dissection. A vertical incision, starting from this first incision at a point 4 to 5 cm. from the midline on the side of neck dissection, is continued downward almost to the clavicle. This incision is made parallel to the opposite sternomastoid (which represents the base of the flap used to repair the esophageal defect), hence it diverges obliquely outward from the vertical. A second transverse incision, passing 2 cm. above the suprasternal notch, extends from the lower end of the vertical incision to the sternomastoid of the uninvolved side.

The parallelogram of skin and platysma so outlined is dissected as far back as the sternomastoid muscle. The larynx is skeletonized by dividing and reflecting the strap muscles, and the isthmus of the thyroid is divided. The trachea is divided through the first or second ring. At this point an endotracheal

tube is inserted and general anesthesia begun (sodium pentathol, nitrous oxide, oxygen is usually quite satisfactory).

Radical neck dissection is carried out on the side with palpable metastatic nodes (or on the side of the primary tumor when no definite nodes are palpable) by reflecting skin flaps above and laterally. The sternomastoid, internal jugular vein and all fatty areolar tissue down to the deep fascia, is removed from below upward. The common and internal carotid arteries, the vagus, phrenic and hypoglossal nerves, the cervical sympathetic trunk, and the thoracic duct on the left, should be preserved. High ligation of the internal jugular just below the jugular foramen is essential since a metastatic node is frequently found high on the posterior aspect of this vein. It is advantageous to ligate and divide the superior thyroid, lingual and external maxillary branches of the external carotid, or the external carotid itself, to facilitate subsequent dissection of the pharynx.

When the neck dissection is complete the upper cervical esophagus and hypopharynx are mobilized in the plane of the loose areolar tissue lying over the prevertebral fascia to a point well above the lesion. The pharynx may be opened laterally or anteriorly in the pre-epiglottic space. It is best to enter on the side of minimum involvement so that resection can be carried out under direct vision as well as palpation. It is permissible to determine the point of pharyngotomy by palpation through the mouth since salivary contamination is inevitable. The pharynx is divided 2 cm. above all visible and palpable tumor. If there is involvement of the vallecula or base of tongue, resection should include this area and the hyoid bone as well. Resection is completed by dividing the esophagus at least 2 cm. (more if feasible) below all palpable tumor.

The skin and platysma flap already prepared is drawn across the midline under moderate tension and anchored to the prevertebral fascia by multiple fine chromic sutures and/or silk or wire retention sutures tied over rubber tubing. The stump of the pharynx is drawn downward and that of the esophagus upward and anchored to the same fascia. The upper border of the skin flap is sutured to the mucosa of the posterior pharyngeal wall by fine silk or wire sutures and this suture is continued until the upper skin margin approximates the entire circumference of the pharyngeal orifice, forming a scroll with the skin inside and the platsyma exposed. Excess skin (if any) may be folded back on itself to cover part of the raw surface of the flap. A similar anastomosis of skin to esophageal mucosa is carried out below leaving a skin lined slot open along the entire lateral aspect.

The long skin flap on the side of neck dissection, which is based on the trapezius muscle, can sometimes be drawn medially to meet the skin edge of the plastic flap. This should not be attempted if any tension is necessary since the blood supply on this side is relatively poor following neck dissection and necrosis is almost inevitable. It is better to anchor this flap to the deep fascia just medial to the carotid, which should be protected, and to cover any remaining raw surface with split thickness grafts.

Prior to closure the permanent tracheostomy is formed by excising a circle of skin in the suprasternal notch and suturing the trachea in place with meticulous care as recommended by Martin[5]. The strap muscles may be imbricated behind the trachea for temporary support, or may be excised. Frequently part of the thyroid must be excised to facilitate closure. Finally, a feeding tube is passed through the nose, pharyngeal stoma and esophageal stoma to the stomach and a firm pressure dressing applied.

After four to six weeks the esophagoplasty may be completed by excising the vertical portion of the scar to mobilize the margin of the skin flap and making a second vertical incision to the opposite side of the midline. Skin is sutured to skin with multiple fine chromic sutures so as to close the lateral opening in the esophagoplasty. The raw surfaces are then covered by split thickness graft. In our experience it is best to delay this a few days to minimize the possibility of losing the graft from infection brought by salivary contamination. Nasal gavage feedings are continued for at least two weeks. If the wound seems well healed, swallowing is then permitted.

CASE REPORT

J. D. CMC No. 5706; Memorial Hospital No. 86119.

A 61-year-old negro male was admitted 2-1-50 with a history of sore throat, earache, dysphagia and weight loss for 12 months. An emergency tracheostomy for severe dyspnoea was performed at the time of admission. Examination showed a bulky cancer involving the right lateral pharyngeal wall, pyriform sinus, arytenoid, aryepiglottic fold, epiglottis and ventricular band. A 2 cm. firm, movable node was palpable over the right carotid bulb. Biopsy from the larynx showed squamous cell carcinoma.

On 2-17-50, after preliminary transfusions and gavage feedings, a right radical neck dissection and excision en bloc of the hypopharynx, upper esophagus and larynx, with first stage esophagoplasty, was performed. The pathologist's report describes a bulky, fungating cancer of the hypopharynx invading the larynx and epiglottis. Two out of 37 cervical nodes examined contained metastatic squamous cancer. On 4-13-50 the esophagoplasty was completed and a split thickness graft applied a few days later. The patient was discharged about four weeks later, his recovery having been delayed by plebothrombosis and femoral ligation following his last operation. His health was good and his swallowing function quite satisfactory on 8-15-50.

DISCUSSION

A review of the 38 cases treated by irradiation indicates that 18 cases must be classified as totally inoperable; 13 cases had fixed, metastatic nodes; 3 had bilateral metastatic nodes; indicating rapid dissemination of disease; 1 patient was too old and feeble to tolerate the operation; 1 patient had distant metastasis. It is believed that the remaining 20 cases might have been amenable to radical surgery of the type described above. Among these 20 cases, 2 had recurrence in the pharynx and upper cervical esophagus, 1 recurred in the base of the tongue, 2 in the thyroid gland, and 1 in the subglottic region. There were probably several other cases with extension to the upper esophagus which were not proven by biopsy or autopsy. All of these cases would fall within the scope of the operation described.

SUMMARY

(1) The anatomy of the larynx and pharynx is reviewed.

(2) Extensive laryngeal cancer usually involves the hypopharynx as well.

(3) Cancer of the hypopharynx rarely is curable by radiation therapy.

(4) A series of advanced laryngeal and/or pharyngeal cancer cases treated by radiation therapy is reported. Of 21 cases treated up to 1945 there is one survivor.

(5) Resection of the larynx, pharynx and cervical esophagus, and if necessary base of tongue, combined with a unilateral radical neck dissection is described.

(6) The reconstruction of the cervical esophagus by skin flaps satisfactorily restores swallowing function.

(7) Four cases of combined resection of the pharynx and larynx with radical neck dissection, three of which were suitable for esophagoplasty, are reported.

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DISCUSSION

DR. W. M. PIERSON (Wilmington): Dr. Hynes has given you a very pessimistic and discouraging prognosis regarding neoplastic diseases of the hypopharynx and extrinsic larynx as treated by radiation therapy. He has also outlined an operation which, it is to be hoped, will obtain cures for this type of disease.

It has not been so long ago since cancer of the esophagus in any location was considered inoperable. However, today carcinoma of the esophagus may be operated upon and is operated upon successfully continually. Dr.

Hynes has undertaken an operation that is painstaking, time-consuming, requires skill and patience, and he is certainly to be commended for his efforts.

As he mentioned, there are very few reports in the literature relative to surgery for neoplastic diseases of these locations. For the most part, a diagnosis of such a lesion is immediately considered inoperable and are referred for radiation therapy. However, what we are after is a cure, even though it may mean sacrificing a part of the anatomy. The patient desires to live as long as possible, and if surgery obtains a cure, then that is what we are after.

Surgery today is successful beyond other days not only because of improvement in technique but also because of the blood bank, of penicillin, of improved anesthesia technique, and in addition, the realization of the importance of the patient being in tip-top shape before operation. The intimation that the patient should have radiation therapy rather than surgical treatment because of lack of proper conditioning is no longer tenable because it is just as important to have these patients in tip-top shape for radiation therapy as it is for surgery. Perhaps many could stand surgery better than they could radiation therapy.

As in cancer in any other location, an early diagnosis is important if we are to obtain cures. Cancer in the locations under discussion is usually visible by direct inspection, or if not by direct inspection by mirror examination, and certainly by direct examination with the esophagoscope. So that a patient presenting symptoms should be investigated completely for an early diagnosis, before the tumor becomes bulky, and when one is more apt to obtain a cure.

The patient Dr. Hynes showed had a very visible tumor that can be seen by merely using a tongue depressor. It was very large.

I congratulate Dr. Hynes on his work; he should be highly commended. He has undertaken a difficult job, and I hope it means cures for some of these patients.

Dr. H. S. Rafal (Wilmington): It has been a privilege to hear Dr. Hynes' report on the results he has obtained on the achievements over cancer by x-ray surgery. It is difficult to be the second discussant in a subject that is so limited, but there are certain factors that might be mentioned.

X-ray therapy has much that is to be desired, and it will probably be agreed that it may take a good many years before the results of this operation can be properly evaluated. I certainly feel that it is still justifiable, because the only other outlet we have, radiation therapy, has certainly left proof that there is more to be desired.

One point that we might hope for is that some new technique of x-ray therapy, or some modification of an old technique, might be developed to produce results which would be so good that we would be very glad to forego this back-breaking job that this operation entails. For example, by rotation of the x-ray therapy, where the patient rotates around the tube, results have been obtained in carcinoma of the esophagus which compare quite favorably with that of radical surgery and which are far better than those obtained previously with conventional x-ray methods. Whether or not this will concur with this particular instance I don't know, but it is something we can keep in mind and at least hope for in the future.

As was readily seen from the diagram and discussion, and description of the operation, it is quite a formidable procedure. It is done on older patients because these tumors occur most commonly in older persons. However, as mentioned by the previous two speakers, modern anesthetic techniques and antibiotics, and liberal use of transfusions, and I think more than anything else, religious attention to details in the preoperative, operative and postoperative phases of the surgical therapy, give us a chance for low mortality in this operation.

We saw here what the technical difficulties were. There was mention that there were weeks of unpleasant work of keeping these things clean and irrigating them out, sucking them out, and keeping the patients going until the reconstructive phase is reached.

I would like to mention briefly a few technical aspects of this. I may be all wrong, but as far as I know, Dr. Hynes in this operation

has included in the scope of the procedure a unilateral radical neck dissection. To my knowledge, this part of the operation has not been incorporated in previous attempts, such as by Dr. Wilkie. I think it is of considerable importance, as Dr. Hynes described it. The tumor had been found in several of the nodes of the dissection, which of course indicates that the operation was necessary, even though perhaps the nodes are not palpable on physical examination. The primary tumor and the lymph nodes should be removed. That would necessitate a bilateral neck dissection. As Dr. Hynes mentioned, this is a treacherous thing to undertake. He has been content with one side.

It is also important to keep in mind that this is at least in part a plastic procedure. That quadrangular flap carries a great deal of responsibility for the success of the operation. It must be handled with kid gloves. The hemostasis must be done with fuss-budget care, and constant vigilance must be maintained at the time of operation to prevent excessive drying of that flap. Also when the flap is brought across to start the first stage closing, certainly all will agree that you must resist very rigidly the temptation to pull just a little bit more, because it is a flap whose blood supply is quite tenuous and even a slightly excessive tension might produce necrosis and set you back weeks in the reconstruction of the pharynx.

It is of course important to get coverage of the carotid artery. It has been reported, and I have had one such personal experience, where mycotic granuloma has led to fatal hemorrhage, and if not to that, often necessitates ligation of the carotid artery, which in an elderly patient such as this is attended by a high mortality rate.

I have one suggestion that has come to mind, and I am certain it has occurred to Dr. Hynes too, where we might borrow a leaf from the book of men who have had extensive experience with surgery of the esophagus, such as Dr. George Pack. In the operating room, before starting to close, microscopic examination of sections taken from the proximate and distal ends of the incized sections be taken immediately so that the surgeon may know with some degree of certainty whether or not he has transected microscopic tumor.

One point, again mentioned by Dr. Hynes, is the problem in hairy individuals of having a beard growing within the new pharynx. Whether or not that would interfere with swallowing has not been the experience in these cases. I believe Wilkie has made a point of it, and he has advocated depilitating doses of x-rays.

DR. HYNES: I have very little to add. I want to thank the discussants for their very kind words. I think they exaggerated.

I don't know what the effect of the hair turned in on a skin flap will be. I talked to and have written to several men who have had experience with the operation. I have heard of one case becoming obstructed from a long gray beard, but most of them say nothing seems to happen. Maybe the hair follicles atrophy when they are closed into a moist dark space; I don't know. I have read somewhere that the dermal grafts used to prepare hernia lose their hair follicles. They all seem to dry up and atrophy. I hope that is what happens to these fellows. If it doesn't, we can give them x-ray treatments to depilate them. Wilkie gives them an epilation dose of x-ray before operating. I think that is risky. I think it is possible to work out a different type of closure, using a split graft, instead of a skin flap, but that hasn't been tried on this sort of case, so I will have to withhold any comments on that point.

With the minimal case of tuberculosis, diagnosis is rarely the clear-cut matter it is in more active, progressive, and advanced cases. It may involve, frequently, the most tedious follow-up and most painstaking analysis and evaluation. These are the lesions which, under normal circumstances, rarely get the doctor's care because of their obscurity and elusiveness—those which may be forever the "silent" lesions in tuberculosis. —Robert J. Anderson, M. D., Journal-Lancet, April, 1950.

SPONTANEOUS HEMOPNEUMOTHORAX*

New Concepts in Treatment

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A review of the experience in the treatment of spontaneous hemopneumothorax on the Chest Service of the Memorial Hospital during the last three years has demonstrated some important features. While spontaneous pneumothorax is relatively common it is not usually complicated by hemorrhage. In a recent review of the subject in the *Annals of Internal Medicine* for September, 1950 by Arst, Lahey, and Kunkel, it was noted that only 60 cases had been reported through 1947.

In 1949 Dorset and Terry[2] reviewed 54 cases and found 14 to be fatal. Most of these died during the course of the first twenty-four hours. In most of the cases the source of bleeding was found in torn pleural adhesions.

In 1942 Hartzell[3] advised that thoracentesis was inadvisable except for diagnosis or for the relief of mediastinal displacement. It was thought that rapid and complete removal of the blood without air replacement was likely to result in renewed bleeding. The withholding of transfusions was advised except in extreme emergency in order that fresh bleeding would not be initiated. The late results of hemopneumothorax were not considered. The work with traumatic hemothorax during the recent war changed the concepts of handling blood in the thoracic cavity, but this concept apparently has not been completely accepted in the medical management of spontaneous hemopneumothorax. Moore[4] felt that the method of choice was complete aspiration as soon as possible and that the injection of air would be contraindicated. It was noted that bleeding in the chest wall could not be controlled by maintaining a pneumothorax and that bleeding of the lung tends to cease spontaneously because of the low pressure in the pulmonary circulation. The incidence of chronic hemothorax and empyema was found to be higher in those patients treated by aspiration and air replacement than in those treated by aspiration alone, during the war. Yet as recently as 1949 Dorset and Terry[2] conservatively suggested that in the first few critical days no more than 200 to 500cc. of blood should be removed and then it should be partially replaced by air. In none of the earlier literature is much stress made of the late complications of hemopneumothorax. In 1949 Nalls and Matthews[5] did suggest that decortication might be necessary in some cases in which the lung cannot fully expand because of clotted blood and a resulting fibrothorax after hemopneumothorax. However, some cases have been reported in which there was no limitation of pulmonary expansion following a hemopneumothorax in spite of the fact that no blood had been aspirated. Nalls and Matthews's case in which a decortication was done did have a good result but the patient had a prolonged and protracted hospital course.

In 1947 the problem of massive spontaneous hemopneumothorax was previously reported from this hospital[6]. In the reported case the bleeding was severe enough to require 4000cc. of blood by transfusion in the first five days in order to control shock and anemia. During the first nine days over 6000cc. of bloody pleural fluid was removed from the right chest. The patient was acutely ill and on several occasions appeared to be in immediate danger. In spite of frequent aspirations of blood, clots did develop in the thoracic cavity and a month after the initial hemopneumothorax it was necessary to decorticate the lung. This patient's course was also protracted and his life seemed to be in jeopardy on several occasions because of the initial management.

In view of these considerations the following is thought to be worthy of detailed discussion:

A thirty-three year old white man was admitted to the Memorial Hospital with a chief complaint of severe pain in the left chest, beneath the scapula. The duration of pain was two hours and it was worse on respiration and on movement of the trunk. The pain began at work when the patient turned around on his desk chair. Almost immediately he had dyspnea and became pale and shocked. For

*From the Chest Service of the Memorial Hospital.

three days previously he had had a cough productive of thick sputum. He had remained at home a couple of days and had returned to work the day of admission, in spite of some continued cough.

Examination on admission showed a very apprehensive patient in acute distress, with labored respirations (rate 28), and with intense chest pain upon any movement of the body. The temperature was 98.6, blood pressure 150/102, and the pulse 92. Chest expansion was limited on the left. No heart sounds were heard over the left chest. Cardiac dullness was percussed two cm. lateral to the right sternal border. The percussion note was tympanitic in the left posterior chest and axilla, with bronchovesicular breath sounds in the right chest. The trachea was questionably shifted to the right. Laboratory work showed RBC. of 5.26; Hb. 15 gms., WBC. 22,000, with 90% segmenters; and normal urine. The chest x-ray revealed a complete pneumothorax in the left chest, with a small amount of fluid present at the left base. The heart was shifted to the right.

About an hour after admission the patient's general condition had become worse with more marked dyspnea and cyanosis. His chest was aspirated at the left base and blood was obtained. None was removed. A needle was then placed in the fourth interspace along the anterior axillary line, because his symptoms were felt to be due to a tension pneumothorax. There was an immediate rush of hissing air upon insertion of the needle which was then attached by rubber tubing to an underwater seal at the side of the bed. The dyspnea and cyanosis improved. In addition to the thoracentesis sedation was given and chemotherapy was started. During the evening of the first day the patient continued to complain of pain on coughing. He was nauseated and vomited several times.

During the morning of the second day blood began to go into the trap bottle when he coughed. X-rays revealed increased fluid in the chest. In the afternoon, even though 500cc. of blood was aspirated, a re-check film showed progressive increase in the fluid. In addition, the drainage bottle was filled with several hundred cubic centimeters of blood. The patient's red blood count dropped to 4.20, with 12.5 gm. of hemoglobin. At 8:30 p. m. 700cc. more of dark red blood was removed, with some relief of the increasing dyspnea. The pain remained around the left shoulder, and analgesics were needed. In spite of blood loss, the patient showed no signs of real shock but he was becoming weaker and his pulse was rapid (around 116) and at times quite weak. Sixty mgm. of vitamin K was given intravenously, empirically, in an effort to control the bleeding.

On the third day the patient was still weaker. His dyspnea and orthopnea were a little more marked. X-rays showed increased fluid in the chest. The blood count in the morning remained about the same. The patient was coughing up some grayish sputum, examination of which showed micrococcus catarrhalis and non-hemolytic streptococcus. Smear was negative for acid-fast organisms. The first blood transfusion of 500cc. was given. The red blood count several hours later was 3.78, with Hb. of 12.5 gms. The pulse continued to be rapid. The patient was perspiring and cool and was felt to be in borderline shock. Plasma was started late in the afternoon. Further laboratory studies by this time showed a coagulation time of six minutes, bleeding time of one minute, and a prothrombin time of 95%. A repeat chest film in the evening and a RBC. of 3.32, with 10 gm. of Hb. confirmed the clinical impression of continued bleeding in the left chest. 1500cc. of blood was then removed, and shortly thereafter the patient was taken to the operating room, where an exploratory thoracotomy was done.

The left lung was found to be completely collapsed with a large amount of jelly-like clotted blood in the chest. (Note — This had been suspected by the roentgenologist preoperatively.) Oozing of blood was present from adhesions in the apex and the left costophrenic angle. Although the oozing was considerable no active bleeding points were seen. There were adhesions between the base of the lung and the parietal pleura. Repeated expansions of the lung under direct vision failed to reveal any other source of bleeding or any air leak. At the apex there was a small protrusion of lung tissue through the visceral pleura but

no definite leak was demonstrated from this point. The bleeding was controlled by ligatures to the adhesions and by the use of multiple gelfoam packs. The herniated bit of lung was inverted beneath a row of sutures. An intercostal catheter was introduced into the thoracic cavity through the ninth interspace at the anterior axillary line. Reexpansion of the lung before closure of the chest wall revealed no areas of leakage. The drainage tube was attached to an underwater drainage system guarded by a negative pressure bottle and by a third bottle to which positive pressure was applied in order to create negative pressure within the left thoracic space.

The patient tolerated the procedure well and was given 1000cc. of blood during the operation. His postoperative course was smooth from the beginning. He maintained his blood pressure. His respiratory movements were good and he had a moderate cough. Breath sounds came through well in the left chest. Because of a continued depression of the RBC. to 3.36 with 9.5 gm. of Hb., he was given 500cc. more of blood on the first postoperative day. A platelet count at this time was reported to be 70,000, but a subsequent clot retraction time of one and a half hours was normal. Later the platelet count increased to 100,000. Postoperative x-rays in the first few days after the thoracotomy showed a complete removal of all the hemothorax material and complete inflation of the left lung.

On the second postoperative day the patient coughed up moderate amounts of grayish black sputum. His temperature reached a peak of 101 degrees. The tube was removed from the chest and he was allowed out of bed with no ill effects.

Re-check x-rays on the third postoperative day showed almost as good airation in the left as in the right lung. The diaphragm was elevated on the left. 500cc. more blood was given, since his RBC remained around 3.16, with 8.5 gm. of Hb.

By the fourth postoperative day he was eating his meals out of bed and walking about the hall. A slight cough continued, but sputum examination again was negative for acid-fast organisms. Culture showed N-catarrhalis and one-hemolytic streptococci.

The patient's course continued favorable and he was finally discharged on the ninth postoperative day, in good condition. An x-ray taken at that time showed the left lung to be completely inflated with a costophrenic angle that was fairly clear. There was no parenchymal infiltration.

The patient returned to work within another week or two and since that time has remained asymptomatic.

Discussion

This thirty three year old man was acutely ill for the first few days. He showed no evidence of improvement with the routine conservative management. His hemorrhage was massive and continued until the time of operation on the third day after admission. Although the bleeding may have been poorly controlled because of a low platelet count, this did not lead to postoperative bleeding. The bleeding was from torn pleural adhesions. (This agrees with the previous evidence concerning the cause of bleeding in some other cases of spontaneous hemopneumothorax). By a relatively simple exploratory thoracotomy the bleeding points were controlled. The use of gelfoam gauze was of undoubted value. Clots had already formed and would have hindered re-expansion of the lung even if the bleeding had been under control. A subsequent thoracotomy for decortication might have been necessary. Thus, in this case our patient was not only spared the possible dangers of uncontrolled hemorrhage but he was saved a long hospital stay, including a subsequent operation. As it was, he left the hospital twelve days after admission in a good state of health and nutrition.

In addition to the cited example, two other cases seen on the Chest Service of the Memorial Hospital emphasize the importance of proper management of hemopneumothorax. One was a twenty-six year old man who had been originally treated conservatively elsewhere for spontaneous hemopneumothorax. He was subsequently referred to the Chest Service because of left anterior chest pain and dyspnea. His original x-rays showed that his pneumothorax was complicated by only minimal bleeding, which was not aspirated. Thoracotomy revealed a fibrin membrane holding the left lower lobe in complete collapse. The

lower lobe was decorticated and re-expanded. The outcome was satisfactory. This case points out that even a small amount of bleeding may lead to complications necessitating subsequent thoracotomy for decortication. This is notable because some authors have maintained that aspiration of the blood is not always necessary.

The other patient was a thirty-two year old man with tuberculosis who had massive bleeding following pneumonolysis of adhesions for collapse therapy. He was treated conservatively by aspirations of over 2500cc. of bloody fluid from the chest and by transfusions of 2500cc. of whole blood within five days. His general nutrition and resistance were impaired by the experience and the tuberculosis later spread to the other side. Subsequent decortication and right upper lobectomy were done in an attempt to control his disease. He died after seven months of illness. Perhaps he might have fared better with an immediate surgical attack on the pleural hemorrhage while his general condition was relatively good.

Since that time several other cases have been explored because of massive bleeding at the time of a spontaneous hemopneumothorax. The operations have all been successful. Several cases have also been treated conservatively by means of aspiration. The cases chosen for thoracotomy are those in which bleeding does not appear to show signs of stopping within the first twenty-four to forty-eight hours, and in whom the bleeding is severe enough to demand frequent blood transfusions to counteract a tendency towards shock.

The first reported case in the literature of spontaneous hemopneumothorax treated by thoracotomy appeared in the March, 1951 *Annals of Surgery*[7] This patient too had an uneventful, uncomplicated recovery.

We initially felt that thoracotomy might well be the treatment of choice for almost all cases of hemopneumothorax, even though the initial bleeding was not too severe, in order to obviate the necessity for a subsequent decortication and the associated prolonged hospitalization. These ideas have now somewhat changed as the result of the use of streptokinase and streptodornase[8] to help prevent clot formation in the chest.

While the reported cases of spontaneous hemopneumothorax are rare, inferences from various articles and personal communications with other institutions would suggest that the condition is far more frequent than one would think from the literature. In other words, any doctor may be called upon to direct the therapy in such an emergency. The proper management should be well known. The reported mortality rate of 25% indicates the seriousness of the condition as treated by previously recommended methods.

SUMMARY

A case of spontaneous hemopneumothorax in a 33-year-old man is presented. The patient had massive bleeding which was not being controlled by conservative management. Therefore, a thoracotomy was done with subsequent expansion of the lung and arrest of the bleeding. The postoperative course was short and uneventful. The case was compared with two others who were similarly very sick during the phase of hemorrhage, but who were treated conservatively and suffered prolonged illnesses and eventual pulmonary decortication. A fourth case was noted of hemopneumothorax following pneumolysis for tuberculosis with long hospitalization under conservative therapy, subsequent operations, and eventual death.

In view of the cases mentioned, a revision of the standard therapy for spontaneous hemopneumothorax has been recommended.

CONCLUSIONS

Our conclusions are that in cases of spontaneous hemopneumothorax careful consideration should be gven to

1. Treatment of shock and transfusions.
2. Early aspiration of blood and air. The latter is especially important in cases of tension pneumothorax.
3. Frequent x-rays, with aspirations as deemed necessary by x-rays and the clinical findings.
4. Exploratory thoracotomy in cases of massive bleeding which is poorly controlled by conservative measures.
5. Early decortication if conservative procedures have not been successful in producing

pulmonary expansion. These conservative procedures should include the use of streptokinase and streptodornase. These drugs may add to the initial bleeding tendency, however, if given too early and should be used with caution.

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RIGHT UPPER MEDIASTINAL LESION*

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The diagnostic problems handled by a Chest Group are frequently answered by extension of usual diagnostic procedures to a finality of completeness and a careful correlation of information so that a satisfactory therapeutic answer is obtained for the benefit of the patient. Diagnosis of the right upper mediastinal lesion does not fall in the above category and therefore requires special procedures for definitive information for accurate therapeutic application.

The right upper mediastinal lesion is usually a space-occupying mass situated above the right main bronchus. It protrudes from the right side of the normal mediastinal shadow and may extend upward to the clavicle or above it. The medial border of this type of lesion is confluent with the mediastinal shadow and does not show a demarcation from the lung. A pulmonary lesion of small size may be moved away from its mediastinal conjunction by artificial pneumothorax and thus be demonstrated to be entirely pulmonary in significance. Many of these lesions are not amenable to this simple procedure, however, and require special efforts in diagnosis.

This case report is made to describe the use of vascular opacification in an attempt to clarify the diagnosis of a right upper mediastinal mass.

The patient was a 57-year-old male of good

*From the Radiological Department, Memorial Hospital.

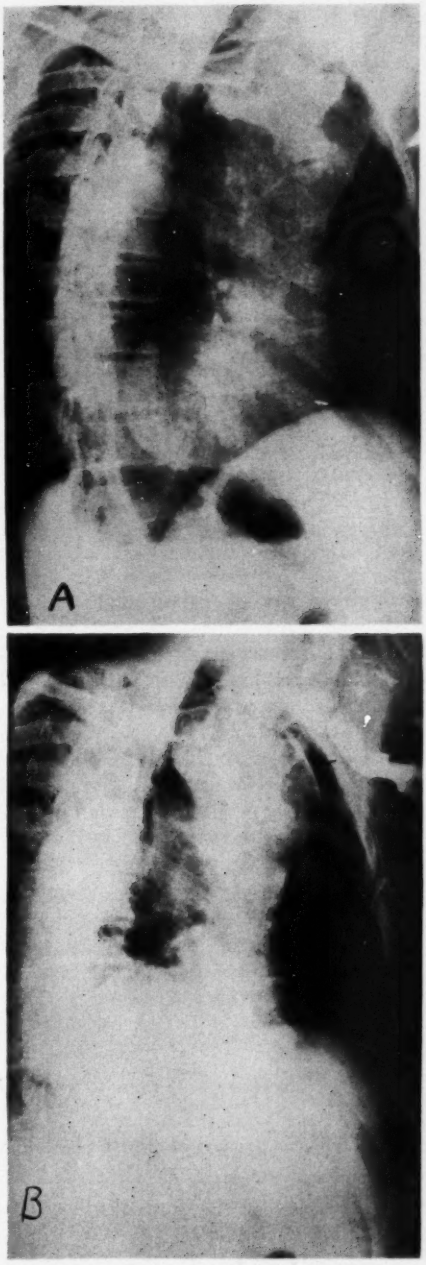

Fig. 1. A—Oblique view before opacification.
B—Inominate aneurysm after opacification.

muscular development and apparent good health. A lesion in his larynx had been demonstrated by biopsy to be a malignant papilloma near the right vocal cord. The x-ray examination of the chest showed a large lesion in the right upper mediastinum, 6x10 cm. The density was almost equivalent to the density of the mediastinal shadow and its location was compatible with the usual pathologic entities to be found in this area. This lesion was considered to be an aneurysm by the examining radiologist in his differential diagnostic outline. The usual procedures of multiplane projections, fluoroscopy, barium swallowing, and the like, did not give definitive diagnostic criterea sufficient to be of absolute value in the determination of therapy.

Vascular opacification was decided upon as a necessary examination in this individual. Contra-indications to the method chosen were ruled out (severe renal or hepatic disease). Technical methods were decided upon and practice dry runs were made by the technical staff of the x-ray Department of Memorial Hospital.

The method chosen was first evolved by Sossman and his group. It allows visualization of vascular structures in a fair degree of accuracy using equipment available in most hospital x-ray departments. In this case report an attempt will be made to outline the clinical approach to this problem of vascular opacification to demonstrate an aneurysm.

TECHNIQUE

The clinical examination of this patient revealed a positive serology and a positive biopsy of a laryngeal lesion. A diagnosis of accurate degree was needed of the chest lesion, to evaluate therapy, on the basis of:

1. Carcinoma of larynx
   Lues
   Luetic aneurysm of inominate artery
2. Carcinoma of larynx
   Carcinoma, primary or metastatic in chest
   Lues

The first step in the procedure was a determination of circulation time:

1. Arm to lung, by ether
2. Arm to tongue, by decholin

These tests were done in the usual manner and the results were:

1. Arm to lung, 15 secs.
2. Arm to tongue, 43 secs.

The arm to lung time was satisfactory, but the arm to tongue time was considered to be abnormally prolonged. Discussion elicited the fact that the patient did not appreciate the decholin taste promptly and a correction was made to 35 secs. (It was not feasible to repeat the decholin time because of previous time schedules in the Department). It was decided that a preliminary taste test should be done with decholin so that a patient could recognize the taste at once. (In a more recent case this preliminary taste testing was very effective). A rough calculation for the taking time of the first film is 25 per cent less than the decholin time, to show the left side of the heart. To show the aorta, the inominate artery, and the descending aorta this time was extended to 20 per cent less than the decholin time. These corrected times were then:

1. Arm to lung, 15 secs.
2. Arm to tongue, 35 secs.
3. Arm to inominate artery, 28 secs.

The second step in the preparatory procedure was an intradermal test with diodrast. Since this test is for allergy, diodrast in thirty-five percent dilution was used. The test was negative.

The actual examination was carried out in the X-ray Department. The patient was seated in front of a stereo-cassette changer. Two films were taken as survey or test films. The position of the patient is important and should be predicated on the location of the lesion. The patient faced the film obliquely with the left chest in contact with the film changer, roughly on an angle of fifty degrees. The right arm was extended to allow intravenous injection. The patient's body was retained in a secure upright position by an eighteen inch wide binder, firmly affixed to the film changer. Test showed that two exposed films could be secured in 0.75 seconds. X-ray technical exposure factors varied but little from usual technique. Fast exposure by fast Bucky apparatus was utilized but is probably not necessary.

Intravenous injection was prepared by Dr. Marvin Dorph, Resident in Medicine at Memorial Hospital. Fifty ml. of 70% diodrast were drawn into a 50 cc. syringe. A 12 gauge needle was to be used on the syringe. At this time a pulse check was made on the patient. An elevation to 120 was noted. The pulse rate at rest was 74-78. The increase was considered to be due to excitement. The increased pulse rate required a correction in the arm to inominate time, previously calculated of 28 secs. A correction of three seconds was made because of the pulse acceleration giving an arm to inominate time of 25 secs.

In the trial runs a counting procedure was evolved, starting with 25 seconds, and using 0 second as the time at which the dye would be in the aneurysm. At 5 seconds before zero the x-ray tube was energized; at 4 seconds the "hold breath" command was given. At one second the first exposure was made and at 0 second, plus one, the second exposure was made. Dr. Dorph was able to inject 50 ml. of diodrast in 1.68 seconds through the 12 gauge needle. The time count was started 1.5 seconds after injection was started.

Two good exposures were secured. The position of the patient made the arch of the aorta parallel with the film plane. The inominate artery was not obscured by the spine shadow and clearest visualization was secured as planned.

Opacification of the mass was evident and the diagnosis of inominate aneurysm was confirmed. This procedure should be considered as vascular opacification and not as angiocardiography . The time sequence is the most important factor. The usual equipment, such as was used in this case, can be used to show the left heart (ventricle), the thoracic aorta, and the abdominal aorta, with sufficient accuracy to make the examination worth the experience to the patient. Right heart angiocardiography does need electrocardiographic control of the timing sequence.

This report is a record of an attempt to differentiate right upper mediastinal lesions, when a vascular abnormality is the primary presumptive diagnosis. The procedure uses equipment found in any hospital X-ray Department. The effect on the patient can be calculated and be made safe by proper precaution. Two good opacified films can be secured to compare with previously taken non-opacified films.

PRIMARY HEPATOMA

Case Report and Brief Discussion of the Disease

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Primary carcinoma of the liver is a rather rare disease and it is thought that a discussion of it and presentation of an illustrative case may be of interest to the profession, as this disease is probably not commonly considered in differential diagnosis of liver lesions, and indeed in this case it was not suspected until found at autopsy.

Case Report

The patient, a 47-year-old, single, negro male, was admitted to the Memorial Hospital on September 25, 1950, complaining of severe para-umbilical burning pain radiating to the epigastrium. The patient was never able to give a completely adequate history, apparently because of impairment of his mental faculties from his severe illness. Nothing relevant was found in his family history or past history except that he had had a previous admission in August, 1948, complaining of shortness of breath for five years and "spitting up blood" for one year. A bronchoscopy was done at that time and the discharge diagnosis was acute suppurative bronchitis.

For about one year prior to the present admission the patient had intermittent, short, crampy, abdominal pains, not localized, and relieved by taking soda, food, or vomiting. He also repeated the history of spitting up blood (whether coughed up or vomited could not be ascertained). For about one week before admission he had right upper quadrant burning pain, which sometimes radiated to his right shoulder. Once during that last week he thought that he vomited a small amount of blood. He gave a rather vague history of a sharp blow to the right upper quadrant of the abdomen on the day before admission. On the morning of admission he was seized with a severe para-umbilical burning pain radiat-

ing to the epigastrium and he then came to the Accident Ward.

There was no history of jaundice, dark urine, abnormal stools, change in bowel habit, weight loss, fever, or alcoholism. Physical examination revealed the patient to be in shock, with cold, damp skin, no blood pressure obtainable, pulse 120, and rather marked pallor of the mucous membranes. There was no jaundice. The tongue and mouth were crusted with dried blood. The heart and lungs were essentially normal. In the abdomen no organs or masses were palpable, but there was moderate tenderness in the epigastrium and the right upper quadrant. Rectal examination showed only slight enlargement of the prostate. The physical examination was otherwise negative.

The impressions on admission were hemorrhage from a peptic ulcer, perforated ulcer, or cholecystitis.

Laboratory tests showed a hemoglobin of 8.5 grams, red blood count 2.9 million, white blood count 9,600, with 85% neutrophiles and 15% lymphocytes. Urine analysis was negative. Blood urea nitrogen was 37. Gastric analysis showed an average amount of hydrochloric acid and there was coffee-ground material in the aspirate but no red blood. Electrocardiogram was negative. X-rays of chest and abdomen gave evidence of right subdiaphragmatic abscess, inflammatory reaction at the base of the right lung, and elevation of the right diaphragm.

The shock was controlled with transfusions, but the patient's abdomen became distended, peristalsis disappeared, pain continued, and the temperature, which was normal on admission, rose to 103° on the third day. A Levine tube was passed and the patient started on penicillin and streptomycin. There was no improvement, so on the fifth day the right subdiaphragmatic area was explored extraperitoneally. A large amount of bright red blood was found, and on inadvertently opening the peritoneal cavity, thin bloody fluid was encountered. The liver appeared grossly to be in the end stage of cirrhosis. No bleeding point was found and there was no evidence of pus, so the wound was packed with gauze and left open. The patient remained in poor condition, and on the third post-operative day the abdomen was clinically filled with fluid and a paracentesis revealed bright red blood. After a transitory improvement, the patient became worse, developing more abdominal distention and profound shock. In spite of transfusions, he died on the thirteenth post-operative day.

The pertinent autopsy findings are as follows: There were about 500 cc. of thin bloody fluid in the right chest. The lungs showed congestion, edema, atelectasis, and bronchopneumonia. There was a massive hemoperitoneum. The mesenteric lymph nodes showed hyperplasia. There were esophageal varices which probably accounted for the history of vomiting blood. The spleen showed moderate hyperplasia and weighed 340 grams. The liver was brownish-yellow, weighed 1,500 grams, was of average size, and was composed of small nodules of liver tissue with connective tissue septa between. The substance was everywhere very soft, particularly in the upper part of the right lobe beneath the diaphragm, where there was a large area of hemorrhage and liquefaction necrosis, presumably the site of the patient's fatal hemorrhage. The gallbladder was negative save for a large calculus.

The important microscopic findings were in the liver and lungs. The liver showed severe portal cirrhosis, and in the necrotic area, there were scattered islands of atypical liver cells with many giant and multinucleated forms and mitotic figures. These bundles of cells infiltrated the liver substance and in some areas showed marked necrosis. The appearance was that of a primary hepatoma. In addition to the findings described in the gross, the lungs showed small deposits of metastatic tumor with tumor cells scattered through blood vessels. Cause of death: Primary hepatoma, with secondary massive hemorrhage.

DISCUSSION

Incidence. Primary carcinoma of the liver is quite common in certain races in Africa and the Orient, but rather rare in Europe and America. This difference is environmental rather than racial, because members of oriental and negro races residing in America do not

show any higher incidence of the disease than is found in the rest of the population.

The incidence in America is about 2% of all carcinomas and it definitely parallels the incidence of cirrhosis of the liver, the higher incidence in other parts of the world being associated with a higher incidence of cirrhosis.

Liver carcinoma occurs predominantly in males from 40-60 years of age in this country, the ratio of males to females being variously estimated at from 2:1 to 12:1.

From 3 to 6% of cirrhotic livers contain primary carcinoma, and of the two types found, it is said that 90% of hepatomas and 50% of cholangiomas arise in livers with cirrhosis, although some investigators are of the opinion that cholangiomas are infrequently associated with cirrhosis. Hepatomas outnumber cholangiomas by a ratio of 6:1 in adults, and in the rare cases which occur in children, almost all are hepatomas. In children the disease is rarely associated with cirrhosis and it usually occurs before the end of the second year of life.

Diagnosis. The symptoms and signs are not diagnostic, but usually consist of a progressive, constant, aching pain in the right hypochondrium, weakness, anorexia, weight loss, moderate leukocytosis, secondary anemia, and irregular fever. If cirrhosis is present, all the manifestations of this disease may be found and may confuse the picture. Aspiration biopsy of the liver may be very helpful in establishing the diagnosis. Jaundice may be present if there is biliary obstruction from metastatic lymph nodes or if biliary cirrhosis is present. The liver may be enlarged and nodules may be palpated in it. The spleen may be enlarged or normal.

Differential Diagnosis. A listing, without details of differentiation, of other conditions to be ruled out is as follows: Portal or biliary cirrhosis, gallbladder disease with or without common duct stone, secondary tumor metastatic to liver, hepatic abscess, echinococcus cyst, benign liver tumor, and sarcoma of liver.

Gross Pathology. The liver may or may not be enlarged, depending on the degree of cirrhosis and the duration and rate of growth of the tumor. There is usually the typical nodular conformation of portal cirrhosis and, in addition, small or large, grayish-red, soft, hemorrhagic and partially necrotic tumor nodules are commonly seen, although gross differentiation from cirrhosis may be impossible. Sharply outlined tumor nodules are often seen in the larger branches of the portal and hepatic veins. Three gross types are described: (1) scattered tumor nodules throughout the liver, the commonest type; (2) the massive type with one large tumor nodule surrounded by a few smaller ones; and (3) diffuse nodulation, often grossly indistinguishable from cirrhosis.

The tendency toward necrosis probably accounts for the fever and leukocytosis, and the pain may be caused by distension of the liver capsule and pressure on surrounding organs.

Microscopic Pathology. The liver cell type, or hepatoma, is composed of clusters and cords of atypical liver cells with a trabecular structure. Many giant and multinucleated forms and numerous mitoses are seen. The cytoplasm is granular and acidophilic and may contain bile.

The bile duct type, or cholangioma, is identical to carcinoma of the extrahepatic biliary system and is an adenocarcinoma composed of columnar cells. Bile is often seen in the lumina, but not usually in the cytoplasm.

Gradations between these two types occur, in which one or the other of the types may predominate.

An academic question arises as to whether liver carcinoma is of unicentric or multicentric origin, some investigators believing that the disease arises at one focus and spreads throughout the liver by way of the hepatic and portal veins, and others maintaining that the carcinoma may arise in multiple areas throughout the liver simultaneously.

Metastases. The common sites for metastases are to the regional lymph nodes, lungs, and tracheobronchial lymph nodes. Direct spread by continuous growth along the hepatic vein, into the inferior vena cava and even up into the right auricle is also encountered.

Treatment. The treatment is very unsatisfactory due to the usually advanced stage of the disease when symptoms first occur, but surgery is occasionally of some value in ap-

parently localized lesions. In none of the publications referred to in preparation of this paper was there any mention of the use of radiation or chemotherapy in the treatment of this disease, but it would seem that these measures might give some palliation.

Prognosis. This is almost hopeless, almost all patients dying within six months from the onset of symptoms. Death is usually due to failure of liver function to which an associated cirrhosis probably contributes to a great degree, but it is not uncommon for death to occur from massive hemorrhage, as in the patient cited above. Among fourteen apparently operable cases collected by Charache from the literature only one survived for more than five years following operation.

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In 1950, our payments for the Hospital Plan totalled $1,657,197.46. Our payments for the Surgical Plan totalled $1,313,327.93. Blue Cross covered 20,644 in-patient hospital cases totalling 160,157 days of care; and 7,076 out-patient cases. Of the hospital cases paid for in 1950—46% were for surgery; 32% were for medical care; and 22% were for maternity care.

U. of P. Dinner

The University of Pennsylvania Medical Alumni Society will hold a dinner meeting Wednesday, June 13, 1951 at Haddon Hall in Atlantic City, in connection with the convention of the American Medical Association. Cocktails 5:30 p. m., dinner at 6:30 p. m. All alumni attending the convention are urged to come to the dinner. Tickets will be on sale Monday and Tuesday at the University of Pennsylvania Alumni Society booth at the entrance to the exhibit hall in Convention Hall.

"Federalese"

A Program—Any assignment that can't be completed by one phone call.

Channels—The trail left by an interoffice memo.

Status Quo—This mess we're in.

To Expedite—To confound confusion with commotion.

Liaison Officer—A person who talks well and listens better, but has no authority to make a definite statement.

To Activate—To make carbons and add names to the memorandum.

Under Consideration—Never heard of it.

Under Active Consideration—We're looking in the files for it.

Conference—A place where conversation is substituted for the dreariness of labor and the loneliness of thought.

Modification of Policy—A complete reversal which nobody admits.

To Spell Out—To break big hunks of gobbledygook down into little hunks of globbledygook.

A Survey is Being Made on This—We need more time to think of an answer.

Further Substantiating Data Necessary — We've lost your stuff. Send it again.

Confidential Memorandum—There wasn't time to mimeograph this.

"See Me," or "Let's Discuss"—Come down to my office, I'm lonesome.

Referred for Appropriate Action—Maybe your office knows what to do with this.

To Give Someone the Picture—A long, confused and inaccurate statement to a newcomer.

Jerry Klutz—*Washington Post*

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This will interest you — our Plan is 'one of the comparatively small number of Plans which were able to meet in full the requirements of the Approval Standards as revised late in 1950' by the Blue Cross Commission. Deepwater Plant—N. J. Plan.

+ Editorials +

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THE PERIOD OF GESTATION

In the press of April 9, 1951 appeared the following item:

CHILD IS BORN AFTER 11-MONTH PREGNANCY

NORRISTOWN, Pa., April 9 (AP).—Doctors at Sacred Heart Hospital yesterday disclosed that a woman had given birth there after a pregnancy of 11 months.

It was one of the rare medical cases of a pregnancy exceeding 300 days in contrast to the normal 280-day period.

The child, a boy, was born April 3 to Mrs. Grace Cartwright, 33, wife of Charles Cartwright, an employe of the circulation department of the Philadelphia Inquirer. The infant weighed eight pounds, three ounces.

This obstetrical anomaly is not new. Williams, in 1909 cited two cases of his own that "did not fall into labor till considerably over eleven months after the last period." Williams also cited Winckel's careful studies showing "that in very exceptional instances pregnancy may last as long as 336 days."

However, such anomalies as these frequently find their way into the divorce courts. Below, we quote the most recent article on this subject, from the London *Lancet*, of December 30, 1950:

MEDICINE AND THE LAW

THE COURTS AND THE PERIOD OF GESTATION

Within limits carefully defined in legal textbooks our courts confess judicial knowledge of certain simple facts of nature without requiring them to be proved by evidence. In Preston-Jones v. Preston-Jones,[1] decided in the House of Lords on Dec. 14, Lord Simonds observed that it had never been doubted that the court had judicial knowledge of the normal period of human gestation.

The normal period, it seems, has been variously stated; it was taken, for example, as 270-275 days in 1887 (Bosvile v. Att. Gen.) and as 273-278 days in 1889 (Burnaby v. Bailie). Subsequent litigation has taught the judges something about abnormal periods. In the Gaskill case in 1921 Lord Birkenhead held that a period of 331 days could not be regarded as impossible in the then state of medical knowledge. In Wood v. Wood, where there was no medical evidence, the Divisional Court took the same view of a period of 346 days. Early in 1949 the Divorce Court allowed even 349 days to be a possibility (Hadlum v. Hadlum[2]). As the number of days continued to rise, the judges clearly found it necessary to draw the line somewhere. In the recent Preston-Jones case the figure of 360 was in effect (though the judges were not unanimous) declared to be on the wrong side of the line.

Mr. and Mrs. Preston-Jones were married in April, 1941; a daughter was born a year later. On Aug. 13, 1946, a second child was born. The husband petitioned for divorce in the following November. He contended that this second child had been conceived between Aug. 29, 1945, and Feb. 13, 1946. During the whole of that time he was absent from the United Kingdom while his wife remained here. He alleged that it was not his child and that its conception was the result of an act of adultery. The divorce commissioner dismissed the husband's petition. The Court of Appeal ordered a re-hearing. The case being reopened, Mr. Commissioner Blanco White found that the husband had been absent from the United Kingdom between Aug. 17, 1945, and Feb. 9, 1946. The wife had suggested that her husband had visited her in the intervening November, but this the commissioner did not accept. He further found that the birth of the child (which weighed 8¼ lb.) was apparently normal and that it could not have been begotten as the result of marital intercourse on or after Feb. 9, 1946, the date on which the husband arrived home. The commissioner had then to ask himself whether the fact that at least 360 days had elapsed between the last possible intercourse between husband and wife and the birth of the child, together with the

medical evidence, put it beyond reasonable doubt that it was not the husband's child. The commissioner, who apparently found the medical evidence inconclusive, held that he would not be justified in finding that the wife had committed adultery; he dismissed the petition. Once more the husband appealed and once more the Court of Appeal directed a re-hearing; it might, it seems, have granted the husband a decree outright, had there not been some question of the admission of certain correspondence at the trial.

By a majority of four to one the House of Lords has now allowed the husband's final appeal and has remitted the case to the High Court in order that the proper decree may be granted.

There remains, however, a further problem of judicial knowledge or ignorance in cases of this kind. By the normal period of gestation the courts mean the time between conception (the union of the male and female cells) and birth. Recent cases have caused the judges to consider the possible interval between coitus and fertilisation. In the Gaskill case it was suggested that this latter interval might be so long as 21 days; in the Hadlum case one of 14 days was referred to. In M.T. v. M.T., in the latter part of 1949, when the divorce judge refused to accept the possibility of a normal healthy baby being born after an interval of 340 days between coitus and birth, a gynaecologist had stated in evidence that he had never heard of an authentic instance of an interval of 21 days between coitus and fertilisation. Lord Simonds asks if judges can, without evidence, take note of the possibility of some such interval. Can they, without evidence, he asks, refuse to entertain the possibility of a 30-day, or 90-day interval between coitus and conception? He thought that ordinary men and women would regard it as a fantastic suggestion that a normal child born 360 days after the last intercourse between husband and wife could be the child of the husband. "It is to me repugnant," said Lord Simonds, "that a court of justice should be so little in accord with the common notions of mankind that it should require evidence to displace fantastic suggestions." In the Preston-Jones case the only medical evidence was that of a doctor whose training and everyday working practice must have made him familiar with the ordinary problems of gestation and birth. This witness admittedly had not studied the problem of the maximum period from the time of coitus to the time of the impregnation of the ovum; but his earlier answers showed that he regarded as impossible an interval which would defer a normal child's birth until 360 days after coitus. The doctor was, in Lord Simonds's opinion, entitled to give that evidence "as a matter of competent medical opinion" even though he had made no special study of the subject. The divorce commissioner was not justified in disregarding the doctor's evidence. He was, as a matter of judicial knowledge, entitled to know that there were abnormal cases of gestation as well as a normal period; but he was not entitled to set his own view of possible abnormality, whether derived from the reported legal decisions or from other sources, against the evidence which he had heard. Having found the facts as stated, the commissioner should have acted on the medical evidence and should have granted a decree of divorce.

E. I. duPont de Nemours & Company
Wilmington, Delaware

April 17, 1951

To the Editor:

In connection with the discussion of Dr. Pennington's article on obesity, Dr. Lewis Flinn has taken occasion to criticize this Company on grounds which are not in accord with the facts. In the interest of fairness and accuracy, if you decide to publish Dr. Flinn's statements in their present form, it is respectfully requested that you add an editorial note correcting the false implication made.

The article in Holiday was not, as is implied, a news release by this organization. The Curtis Publishing Company had gathered some data outside and had decided to publish the article on diet when they first approached us. We had no latitude to "allow" it or otherwise. As you know, an editor may publish whatever he sees fit, and all anyone can do about it is to present facts which may help counteract inaccurate information which the editor has received elsewhere. The style in which an article is written is a matter of editorial policy entirely.

It seems Dr. Flinn must be aware that we have in this country a free press. His statements in the discussion do not seem to be in accord with such an awareness on his part, and it is difficult to understand what motivated him to make them. That is his own responsibility however, and I am merely writing to you as an editor who, I have every reason to believe, is interested in fairness and accuracy.

Yours very truly
MEDICAL DIVISION
G. H. Gehrmann, M. D., Med. Dir.
Allan J. Fleming, M. D.
Asst. Medical Director.

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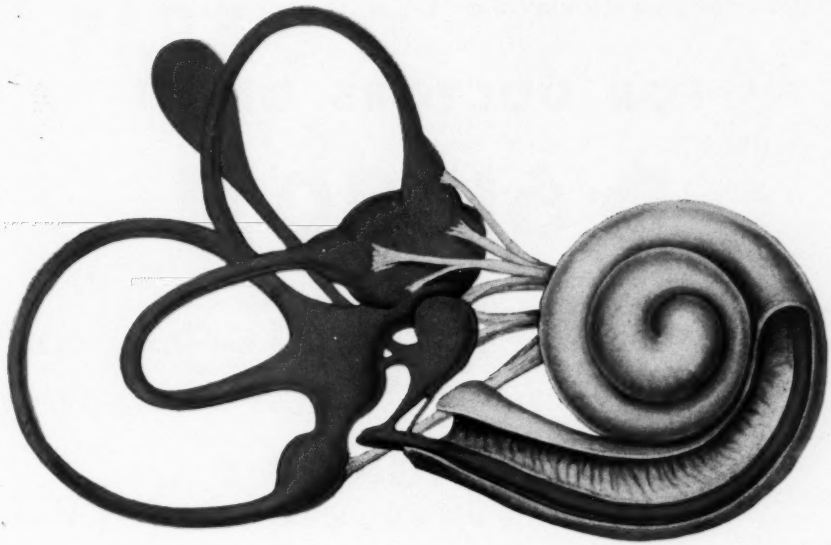

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—Tuttle, A. D.: Special Breakdown of Case Histories, presented at the Airlines Medical Directors Association Meeting, New York, N. Y., Aug. 28, 1949.

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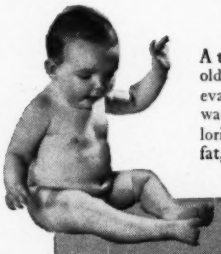

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